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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/620,840	07/21/2000	Lance E. Steward	D-2885	4487

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EXAMINER	
HAYES, ROBERT CLINTON	

ART UNIT	PAPER NUMBER
1647	22

DATE MAILED: 11/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/620,840	Steward et al
Examiner	**Art Unit**
Robert C. Hayes, Ph.D.	1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jul 7, 2003*.

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *44, 45, 47-56, and 58-64* is/are pending in the application.

4a) Of the above, claim(s) *54* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *44, 45, 47-53, 55, 56, and 58-64* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☒ Claims *44, 45, 47-56, and 58-64* are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Response to Amendment

1. The amendments filed 4/03/03 and 7/07/03 has been entered.

2. The rejection of claims 10-11 & 26-31 under 35 U.S.C. 112, second paragraph, as being indefinite for the recitation of "substantially derived" is withdrawn due to the cancellation of these claims.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Applicant's arguments filed 4/03/03 and 7/07/03 have been fully considered but they are not deemed to be persuasive.

5. Applicant's election with traverse of Group I for serotype A, as it relates to only SEQ ID NO:2, in Paper No. 21 is acknowledged. The traversal is on the ground(s) that "since all botulinum toxins are believed to operate by a similar mechanism of action, a search performed for botulinum toxin type A would encompass all of the botulinum toxin serotypes ". This is not found persuasive because the elected invention is directed toward a specific product, as illustrated by its unique SEQ ID NO, in which the search alternatively would not be directed

toward "similar mechanism[s] of action". Therefore, Applicants' arguments are not persuasive, and for the reasons made of record in Paper No.20 (mailed 6/03/03). It is further noted that no Schantz reference has been submitted by Applicants, in contrast to their assertions on page 6 of the response, which is nevertheless immaterial to the instant restriction requirement. The requirement is still deemed proper and is therefore made FINAL.

Claim 54 and claims directed toward different SEQ ID NO are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 16.

6. Claims 44-45, 47-53, 55-56 & 58-64 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons made of record in Paper No. 17 (mailed 12/31/02) for cancelled claims 1, 6-11 & 26-31, and as follows.

Analogous to the situation decided in *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993), "an adequate written description of a DNA [product] requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself". *Fiddes v. Baird*, 30 USPQ2d 1481, 1483 (1993) held that claims directed to mammalian FGF's were found unpatentable due to lack of written

description for the broad class, in which the specification had provided an adequate description of only the bovine sequence. Similarly, only the specific mutation of adding or deleting SEQ ID NO:2 within the serotype A botulinum toxin has been described in the instant specification.

In addition, the court held in *Univ. California v. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997) that:

"One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is".

and that:

"A description of a genus of cDNAs [products] may be achieved by means of a recitation of a representative number of cDNAs [products], *defined by nucleotide sequence*, failing in the scope of the genus or of a recitation of structural features common to the members of the genus, *which features constitute a substantial portion of the genus* [emphasis added]. This is analogous to enablement of a genus under 112, [first paragraph], by showing the enablement of a representative number of species within the genus. See Angstadt, 537 F.2d at 502-03, 190 USPQ at 218".

In contrast, an invitation for others to discover a representative number of species with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics has not reasonably been provided within the instant specification. Thus, Applicants were not reasonably in possession of the claimed genus of modified botulinum serotype A toxin proteins at the time of filing the instant application; especially as it relates to any undefined/undescribed "first", "second" or "third" regions, or recombinant molecules encoding such, for the reasons made of record in the previous Office action.

Applicant is again directed toward the Revised Interim Utility and Written Description Guidelines, Federal Register, Vol.64, No.244, pages 71427-71440, Tuesday December 21, 1999.

7. Claims 44-45, 47-53, 55-56 & 58-64 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for specific modified BoNT/A neurotoxin proteins with a definable sequence change and a definable and assayable function, does not reasonably provide enablement for any uncharacterized "structural modification" with no assayable and recited function. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims, for the reasons made of record in Paper No. 17 (mailed 12/31/02) for cancelled claims 1, 6-11 & 26-31, and as follows.

In contrast to Applicants assertions on page 6 of the 4/03/03 response, the claims still fail to recite any specific definable structural and functional characteristics by which the skilled artisan would know how to make and use the modified botulinum toxins claimed. Therefore, Applicants' arguments are moot, for the reasons made of record in the previous Office action.

8. Claims 44-45, 47-51, 53, 55-56 & 58-63 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite and incomplete for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the reasons made of record in Paper No. 17 (mailed 12/31/02) for cancelled claims 1, 6-11 & 26-31, and as follows.

Again, it is ambiguous what metes and bounds exactly constitutes a "modified" neurotoxin, in that no "structural modifications" are recited in the claims for determining what constitutes something structurally different; especially for determining when such modifications are "effective to **alter** [some *undefined*] *biological persistence*" (e.g., as it relates to claim 44), or for determining how such can alternatively be "reduced relative to...." (e.g., as it relates to claim 49) when nothing is specifically recited in the claims for comparison with this otherwise relative term.

9. Claims 44-45, 47-53, 55-56 & 58-64 are rejected under 35 U.S.C. 102(b) as being anticipated by Johnson et al. (US Patent 5,939,070; IDS Ref #1), for the reasons made of record in Paper No. 17 (mailed 12/31/02) for cancelled claims 1, 6-11 & 26-31, and as follows.

In contrast to Applicants' assertions, no distinguishable structural and functional limitations are recited in the instant claims that distinguishes Johnson's modified serotype A botulinum toxin from that claimed. Therefore, Applicants' arguments are moot.

In summary, Johnson et al. teach a modified Clostridial botulinal serotype A neurotoxin that is structurally modified to separate the H and L chains (cols. 8-9; as it relates to claims 1 & 10-11), and therefore, still includes a leucine-based motif (i.e., as it relates to claims 6-7 & 26-27) as well as a first, second and third region as recited in claim 10. Because of this structural chain separation modification, the biological persistence/biological half life of the modified neurotoxin is reasonably reduced; absent evidence to the contrary (e.g. see pg. 13 of the

specification; as it relates to claims 8-9 & 29). In the Clostridial neurotoxin was isolated from a naturally existing Clostridial neurotoxin (e.g., col. 7), the limitations of claim 31 are met. In that columns 11-14 teach recombinant production of this neurotoxin and individual domains thereof, the limitations of claim 30 are also anticipated.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Robert Hayes whose telephone number is (703) 305-3132. The examiner can normally be reached on Monday through Thursday, and alternate Fridays, from 8:30 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert C. Hayes, Ph.D.
November 6, 2003

GARY KUNZ
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600